II. REMARKS

Claims 2-11 and 14-16 are pending. Claims 14 and 16 are amended. No new matter is added.

I. The Objection to Claims 14 and 16

The Final Office Action objects to claims 14 and 16 for an informality. In response, Applicants submit that the amendment to claims 14 and 16 obviates any basis for the objection thereto.

II. The Rejections Under 35 U.S.C. § 102

The Final Office Action rejects claims 2-5, 8, 9, 11 and 14-16 under 35 U.S.C. § 102(b) as being anticipated by Walker et al. 1994, Pirttila et al. 1994, WO0162801, or Naslund et al. 1994. The Final Office Action also rejects claims 2, 5, 8 and 14-16 under 35 U.S.C. § 102(b) as being anticipated by Solomon et al. 1996, and under 35 U.S.C. § 102(a) as being anticipated by Huse et al. 2002. In particular, the Final Office Action asserts that "Applicant fails to provide side-by-side comparisons to demonstrate that the claimed antibody is different from those antibodies disclosed by [the cited references]… Applicant has provided no showing that the antibodies in the art have characteristics different from those specified by Applicant and do not in fact cross react with the full length Aβ1-40/42 in the same titration or at the same concentration…" Applicants respectfully traverse the rejection.

None of the cited references disclose or suggest a monoclonal antibody having (1) an epitope encompassing Aβ11-15/17, (2) a reactivity to Aβ11-x, and (3) no cross-reactivity to Aβ1-40, as claimed.

The monoclonal antibodies 10D5 (Walker et al.), 4G8 (Pirttila et al.), BNT77 (Huse et al.), and 6E10 (Naslund et al.), respectively, were obtained from Hyman et al., Kunitz protease inhibitor-containing amyloid β protein precursor immunoreactivity in Alzheimer's disease, Journal of Neuropathology and Experimental Neurology, 51(1), pp. 76-8 (1992), Kim et al., Production and characterization of monoclonal antibodies

reactive to synthetic cerebrovascular amyloid peptide, Neuroscience Research Communications, 2(3), pp. 121-130 (1988), Asami-Odaka et al., Long amyloid β protein secreted from wild-type human neuroblastoma IMR-32 cells, Biochemistry, 34, pp.10272-10278 (1995), and Kim et al., Detection and quantitation of amyloid β-peptide with 2 monoclonal antibodies, Neuroscience Research Communications, 7(2), pp. 113-122 (1990), respectively. Copies of each of these references are attached for the Office's review.

The attached references lend support that the references cited in the Final Office Action do not disclose a monoclonal antibody having (1) an epitope encompassing Aβ11-15/17, (2) a reactivity to Aβ11-x, and (3) no cross-reactivity to Aβ1-40, as claimed. Each antibody asserted by the Office will be discussed below.

10D5 (Walker et al.). Hyman et al. (1992) discloses the raising of monoclonal antibody 10D5 against a synthetic peptide containing residues 1-38 of the amyloid β protein. See Materials and Methods at pages 76-77. Hyman et al. (1992) discloses that immunoblot analysis suggests that the epitope for monoclonal antibody 10D5 may be located within the first 15, or within the first 12 residues of the amyloid β protein. See page 78.

BNT77 (Huse et al.). Asami-Odaka et al. discloses an investigation of the cellular mechanisms underlying the generation of short and long amyloid β protein. See Abstract. Asami-Odaka et al. discloses that BNT77, which consitsts of residues 11-28 of amyloid β protein were emoloyed in the investigation. See page 10273. Asami-Odaka et al. discloses that BNT77 did not react to amyloid β protein residues 17-24 or 17-28, suggesting that its epitope is located in the N-terminal side of amyloid β protein 11-28. See page 10273. Asami-Odaka et al. discloses that a sandwich ELISA system for measuring amyloid β protein 1-40 or amyloid β protein 1-42 that possesses a truncated or amino-acid substitution N-terminus employing BNT77 was developed. Id.

4G8 (Pirttila et al.). Kim et al. (1988) discloses that monoclonal antibody corresponding to a 24 amino acid sequence of cerebrovascular protein were obtained after fusion of mouse myeloma cells with speen cells from SCVAP immunized Balb/c mouse.

See Abstract. Kim et al. (1988) discloses that although monoclonal antibody 4G8 reacted with residues 1-24, 6-24 and 17-24 of the amyloid β protein, it did not react with residues 1-5 or 6-16. See Table I at page 125. In addition, Kim et al. disclose that "All the Mabs reactive to residue 17-24 listed in Table I [including 4G8] effectively competed with each other and, therefore, appear to be directed either against the same epitope, or overlapping epitopes present in the amino acid sequence of 17-24". See page 126.

6E10 (Naslund et al.). Kim et al. (1990) discloses that the monoclonal antibody 6E10, which is specific for the first 17 amino acid residues of the amyloid β peptide, was obtained after fusion of mouse myeloma cells with spleen cells from B1-17 immunized Balb/c mouse. See Abstract. Kim et al. (1990) discloses that although monoclonal antibody 6E10 reacted with residues 1-17, 1-24 and 1-42 of the amyloid β protein, it did not react with residues 1-10 or 8-17, suggesting that "the amino acid sequences in the middle of Aβ 1-17 including the 11th amino acid may be the location of the epitope for [monoclonal antibody 6E10]". See Table 1 at page 117 and pages 117-118.

WO0162801 discloses that monoclonal antibody 266 is raised against the Aβ13-28 immunogen and has Aβ19-23 as an epitope. Solomon et al. discloses that monoclonal antibody AMY-33 and monoclonal antibody 6F/3D are raised against the Aβ1-28 and Aβ8-17 immunogens and is silent with regard to the epitopes of AMY-33 and 6F/3D.

For ease of reference, below is a Table showing a side-by-side comparison of the structure and properties of the monoclonal antibodies cited in the references with the monoclonal antibody recited in the claims.

ANTIBODY	CELL	IMMUNOGEN	EPITOPE	REACTIVITY
Applicants	J&JPRD/hAß11/1 (29B5)	Aβ11-15	Aβ11-15	Aβ11-15/11-x Not Aβ1-40/42
Applicants	J&JPRD/hAß11/2 (5C4)	Aβ11-17	Aβ11-17	Aβ11-17/11-x Not Aβ1-40/42
10D5	Not specified	Aβ1-38	Aβ1-12	Aβ1-38
4G8	Not specified	Aβ1-24	Aβ17-24	Aβ1-24/6-24/17-24/1-40/

				11-40/1-34/11-34 Not Aβ1-5/6-16
266	Not specified	Aβ13-28	Aβ19-23	Aβ1-28/12-28/17-28/16-25/1-42 Not Aβ1-20/10-20/22-35
6E10	Not specified	Aβ1-17	Middle of Aβ1-17	Aβ1-17/1-24/1-42 Not Aβ1-10/8-17
BNT77	Not specified	Aβ11-28	N-terminal of Aβ11-28	Aβ11-40/11-42/1-40 Not Aβ17-24/17-28
AMY-33	Not specified	Aβ1-28	Not specified	Aβ1-40
6F/3D	Not specified	Aβ8-17	Not specified	Aβ1-40
CTLA-4	5C4	CTLA-4	Not specified	CTLA-4

As demonstrated in the Table and as discussed above, none of the cited references disclose or suggest a monoclonal antibody having (1) an epitope encompassing Aβ11-15/17, (2) a reactivity to Aβ11-x, and (3) no cross-reactivity to Aβ1-40, as claimed. Thus, the cited references do not anticipate the claimed invention. Reconsideration and withdrawal of the rejections under U.S.C. § 102 are respectfully requested.

III. The Rejection Under 35 U.S.C. § 103

The Final Office Action rejects claims 2-5, 8, 9, 11 and 14-16 are rejected under 35 U.S.C. § 103(a) as being obvious over Huse et al. 2002 in view of Walker et al. 1994 and WO0162801.

As discussed in the above Section II, neither Huse et al., Walker et al. Nor WO0162801 disclose or suggest the claimed anbibodies. Reconsideration and withdrawal of the rejection under U.S.C. § 103 are respectfully requested.

IV. The Rejections Under 35 U.S.C. § 112, 1st ¶

The Final Office Action rejects claims 14 and 16 under 35 U.S.C. § 112, first paragraph, as lacking enablement. In particular, the Final Office Action asserts that "the

specification fails to provide sufficient guidance as to whether [all of the recited disease conditions] can be diagnosed by the claimed method with the claimed antibody." Applicants respectfully traverse the rejection.

Applicants submit that one skilled in the art would apprciate that amyloid plaques and amyloid deposits are characteristics in the brains of individuals with Alzheimers, Down's Syndrome, Diffuse Lewy Body Disease and Hereditary Cerebral Hemorrhage with Amyloidosis of the Dutch-Type. Further, immunohistochemistry studies have identified Aß11-40 as a major species in the brains of individuals with Alzheimers and Down's Syndrome. See, e.g., the specification at paragraphs [0004]-[0006]. Thus, a person skilled in the art could correlate the formation of amyloid plaques containing Aß11-40 with the development of the recited diseases.

Reconsideration and withdrawal of the rejection under U.S.C. § 112, first paragraph, are respectfully requested.

IV. The Rejections Under 35 U.S.C. § 112, 2nd ¶

The Final Office Action rejects claim 16 under 35 U.S.C. § 112, second paragraph, as being indefinite. In particular, the Final Office Action asserts that "the specification fails to define/describe what is encompassed by the definition of 'support'." Applicants respectfully traverse the rejection.

Applicants submit that the term 'support' is well known in the art and is clearly defined in paragraph [0065] of the specification. For example, a solid support may be polymeric beads, dip sticks, plates or filters. Therefore, the specification has met the metes and bounds of the term 'support'.

Claim 16 is amended to clarify 'solid support'. Reconsideration and withdrawal of the rejection under U.S.C. § 112, second paragraph, are respectfully requested.

VI. The Rejection Under 35 U.S.C. §§ 102/103

The Finaol Office Action rejects claims 2, 6, 7, 15 and 16 under 35 U.S.C. §§ 102(e)/103(a) as anticipated by or obvious over U.S. Patent No. 6,984,720 ("the '720 patent"). The Office asserts that the antibody CTLA-4 disclosed in the '720 patent has the same property and function as the claimed antibody to Aβ11-15/17. Applicants respectfully traverse the rejection.

As shown in the Table in section II above, the hybridoma cell line 5C in the '720 patent produces antibodies specific to human CTLA-4, a T cell surface molecule. The '720 patent does not disclose or suggest that the monoclonal antibody specifically recognizes Aβ11-15/17 as recited in claims 2, 6, 15 and 16. Also, the '720 patent does not disclose or suggest the hybridoma cells J&JPRD/hAβ11/1 and J&JPRD/hAβ11/2 expressing the monoclonal antibody specific to Aβ as set forth in claim 7.

Since the cited document does not expressly or implicitly make any connection between Aβ peptide and diseases associated with production of Aβ including AD, a person skilled in the art would not be able to use the disclosure of the '720 patent to obtain the claimed antibodies and hybridoma cell lines without the knowledge of the present application.

Reconsideration and withdrawal of the rejection under 35 U.S.C. §§ 102(e)/103(a) are respectfully requested.

VII. The Rejection Under 35 U.S.C. § 103

The Final Office Action rejects claims 2-11 and 14-16 under 35 U.S.C. § 103(a) over Huse et al. 2002 in veiw of Walker et al. 1994, WO1602801 and further in veiw of U.S. Patent No. 6,984,720.

As discussed above, the cited references do not disclose or suggest the a monoclonal antibody having (1) an epitope encompassing Aβ11-15/17, (2) a reactivity to Aβ11-x, and (3) no cross-reactivity to Aβ1-40, as claimed.

Reconsideration and withdrawal of the rejection under 35 U.S.C. § 103 are respectfully requested.

VIII. Conclusion

Early consideration and prompt allowance of the claims are respectfully requested. Should the Office require anything further, it is invited to contact Applicants' representative at the telephone number below.

Respectfully submitted,

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